but a difficult one in the borderline case," and that by reason of the application of varying factors "there is a great deal of confusion among the decisions" as to the meaning of such term. 1 Moore's Federal Practice, 2d ed. ¶ 0.142[5.-3].

In the Court's opinion, the factual foundation for venue having been challenged by defendant, it is incumbent upon plaintiff to support the laying of venue in this district. This has not been done.

These considerations as to venue are independent of the issues as to sufficiency of service. Venue is a matter of amenability to suit in a particular district. Sufficiency of service involves the question as to whether a defendant otherwise subject to suit has been properly summoned before the court.

Rule 4 of the Federal Rules of Civil Procedure controls on the matter of process. Rule 4(d)(3) governs on corporate service, and provides that service may be made:

> * * * by delivering a copy of the summons and of the complaint to an officer, a managing or general agent, or to any other agent authorized by appointment or by law to receive service of process.

As to the territorial limits of effective service, Rule 4(f) provides that "all process other than a subpoena may be served anywhere within the territorial limits of the state in which the district court is held, and, when authorized by a statute of the United States or by these rules, beyond the territorial limits of that state. Rule 4(c) applies to "service upon party not inhabitant of or found within state". It provides that:

> Whenever a statute of the United States or an order of court thereunder provides for service of a summons, * * * upon a party not an inhabitant of or found within the state in which the district court is held, service may be made under the circumstances and in the manner prescribed by the statute or order, or, if there is no provision therein prescribing the manner of service, in a manner stated in this rule. Whenever a statute or rule of court of the state in which the district court is held provides (1) for service of a summons, * * * upon a party not an inhabitant of or found within the state * * * service may in either case be made under the circumstances and in the manner prescribed in the statute or rule.

From affidavits submitted on behalf of defendant, it appears that Mr. Meister, upon whom service was made, is a local sales representative of defendant of quite limited authority. Mr. Meister is clearly not an officer, managing or general agent, or otherwise authorized to receive service of process. Consequently, service upon him must fail.

The reason that the Court has entered into a review of the law generally applicable to matters of venue and process is that, while there is but a specific issue before the Court at this time, it does appear to the Court that plaintiff may never be able to require defendant to submit to suit in this jurisdiction. That contingency must be taken into account at this time.

[3] From defendant's affidavits, it appears that there is no representative of defendant within the territorial limits of the Court's jurisdiction upon whom service could be made as an officer, managing or general agent, or person authorized to receive service. Consequently, any possible effective service would have to be extraterritorial. The Court has not found any statute of the United States which would authorize such service in this case. Basically speaking, the Ohio long-arm statute, O.R.C. § 2307.382, applies to causes of action which arise from acts bearing some relationship to the State of Ohio. The claim asserted herein would not come within the terms of that statute.

Therefore, while it is *possible* that venue may exist in this case by reason of defendant's general business activities in Ohio, it appears highly unlikely that plaintiff can effect service upon defendant in such manner as to require defendant to submit itself to the court's jurisdiction. While the Court is sympathetic to plaintiff's claim that he cannot effectively prosecute this pro se action in any other jurisdiction, the Court cannot exercise personal jurisdiction where it does not exist.

Under these circumstances, service is quashed upon Mr. Meister; plaintiff shall within forty-five days either procure good service upon defendant, or consent to a transfer of this action as proposed by defendant; if plaintiff does not effect service or consent to transfer, the action shall be dismissed for want of prosecution.

Court of Customs and Patent Appeals

In re LANGER

No. 9239 Decided Oct. 3, 1974

PATENTS

1. Pleading and practice in Patent Office — Rejections (§54.7)

Even though effective date, for prior art purposes, of many of the references is subsequent to applicant's earliest filing date, references are properly cited for purpose of showing a fact.

2. Patentability — Utility (§51.75)

Specification — Sufficiency of disclosure (§62.7)

Specification containing disclosure of utility corresponding in scope to subject matter sought to be patented must be taken as sufficient to satisfy utility requirement of 35 U.S.C. 101 for entire claimed subject matter unless there is reason for one skilled in the art to question objective truth of statement of utility or its scope; assuming that sufficient reason to question statement of utility and its scope exists, rejection for lack of utility under section 101 is proper; rejection can be overcome by proof indicating truth of statement of utility and its scope as found in specification.

3. Patentability — Utility (§51.75)

It is not proper for Patent Office to require clinical testing in humans to rebut prima facie case for lack of utility when pertinent references which establish the prima facie case show in vitro tests and when they do not show in vivo tests employing standard experimental animals; while full scale clinical trials in humans may be necessary to establish commercial usefulness of dentifrice, development of a product to extent that it is presently commercially salable in market place is not required to establish usefulness within meaning of 35 U.S.C. 101.

4. Court of Customs and Patent Appeals — Briefs (§28.05)

Counsel's argument at oral hearing cannot take the place of evidence.

Particular patents—Dentifrice

Langer, Dentifrices and Method for Reducing Enamel Solubility, rejection of claims 1, 3 to 6, 8 to 11, 13 to 16, and 18 to 20 of application affirmed; rejection of claims 2, 7, 12, and 17 reversed.

Appeal from Board of Appeals of the Patent Office.

Application for patent of Horst G. Langer, Serial No. 29,281, filed Apr. 16, 1970; Patent Office Group 120. From decision rejecting claims 1 to 20, applicant appeals. Affirmed as to claims 1, 3 to 6, 8 to 11, 13 to 16, and 18 to 20; reversed as to claims 2, 7, 12, and 17.

BERND W. SANDT and THEODORE POST, both of Midland, Mich., for appellant.

JOSEPH F. NAKAMURA (JACK E. ARMORE of counsel) for Commissioner of Patents.

Before MARKEY, Chief Judge, and RICH, BALDWIN, LANE, and MILLER, Associate Judges.

LANE, Judge.

This appeal is from the decision of the Patent Office Board of Appeals, adhered to on reconsideration, affirming the rejection of all the claims, claims 1-20, for "lack of proof of utility (operativeness) of the claimed subject matter for its intended purpose" under 35 U.S.C. 101, of patent application Serial No. 29,281,[1] filed April 16, 1970, for "Dentifrices and Method for Reducing Enamel Solubility." We reverse in part and affirm in part.

The Specification

Appellant's specification describes the invention in the following way:

> The present invention concerns compositions and methods using a new source of stannous[2] tin for incorporation in dentifrices by which term is meant mouth washes, tooth pastes, tooth powders and chewing gums, i.e., compositions for introduction into the oral cavity as cleansing compositions.
>
> The novel dentifrices contain tin in the stannous form as a substantially water-insoluble, non-ionizing chelate[3] of a synthetic amino carboxylic acid having an Sn:N ratio of the chelate moieties of 1:1, in the amount of 0.00001 to 15 weight percent. The dentifrices of this invention thus make possible a method for supplying and contacting tooth enamel several times daily with a minor to trace source of reactive tin which reacts with exposed tooth enamel to form a highly insoluble basic stannous phosphate.
>
> * * *

[1] This application is a continuation-in-part of application Serial No. 790,469, filed January 10, 1969, which was a continuation-in-part of application Serial No. 714,411, filed March 20, 1968, which was a continuation-in-part of application Serial No. 359,778, filed April 14, 1964, which was allegedly a continuation of application Serial No. 165,962, filed January 12, 1962, and application Serial No. 43, filed January 4, 1960. The record indicates that The Dow Chemical Company is the real party in interest.

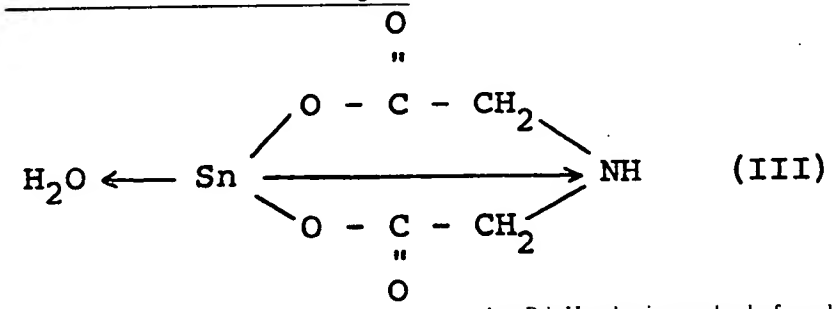
[2] "Stannous" means "of, relating to, or containing tin [chemical symbol: Sn]—used esp. of compounds in which this element is bivalent [Sn^{2+}] * * *." Webster's Third New International Dictionary of the English Language, Unabridged, 2225 (1966). "Stannic" refers to "* * * compounds in which this element is tetravalent [Sn^{4+}] * * *". *Id.*

[3] "Chelate" means "[t]he type of coordination compound * * * in which a central atom (usually a metal) is joined by covalent bonds to two or more other atoms of one or more other molecules or ions (called ligands), so that heterocyclic rings are formed with the central (metal) atom as part of each ring. Ligands * * * offering two groups for attachment to the metal are termed bidentate (two-toothed); three groups, tridentate, etc." The Condensed Chemical Dictionary, 190 (8th ed. 1971).

An effective amount of topical application of stannous tin for the purpose of enamel solubility reduction can be had by employing as a component of the novel dentifrices herein taught at least 0.00001 weight percent of a stannous chelate of a chelating agent corresponding to the following general formula:

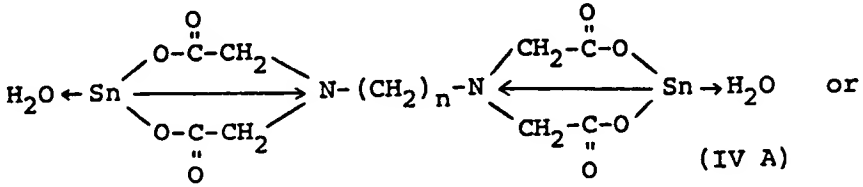
$(HOOCCH_2)_2NR$ (I)

wherein R is selected from the group consisting of H and $[(CH_2)\ n\text{-}N\text{-}(CH_2COOH)]\ m\ CH_2COOH$ (II) wherein n represents an integer which is 2, 3, or 4 and m represents an integer which is 0, 1, 2, 3, or 4, and of the alkali metal salts of such chelating agents, wherein one or two of the $-CH_2COOH$ groups may be replaced by a $-CH_2CH_2OH$ group, resulting in a stannous tin chelate represented by the formula

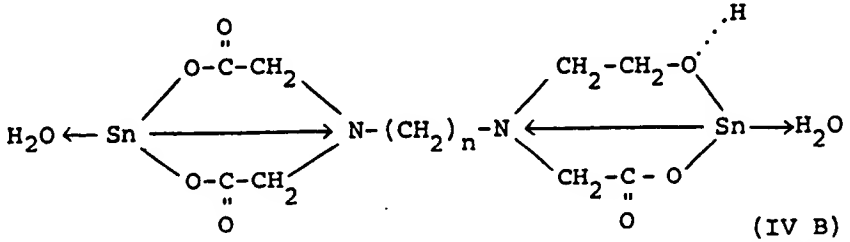


(III)

when R is H and m is zero; by the formula

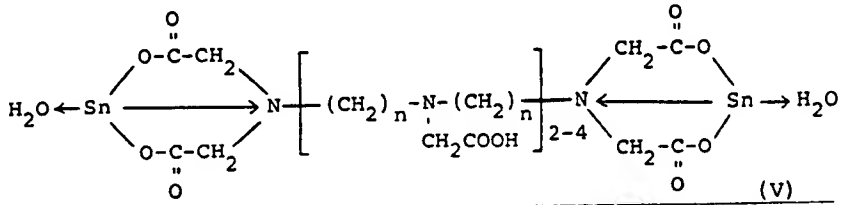


(IV A)



(IV B)

when m is 1; and by the formula



(V)

wherein 1 or 2 of the $-CH_2COOH$ groups may be replaced by a $-CH_2CH_2OH$ group when m of moiety (II) above is 1,2,3, or 4. All of such stannous chelates are substantially water insoluble, i.e., have a water solubility generally less than one percent by weight at room temperature, all the chelate moieties have an Sn to N ratio of 1 to 1, and all provide a source of tin reactive with tooth enamel when introduced into the oral cavity as chewing gum or other dentifrice, to reduce the enamel solubility.

Representative of the foregoing stannous chelates are distannous chelate of ethylenediaminetetraacetic acid [4] (Sn_2EDTA) [also referred to as Sn_2(II) EDTA]; distannous chelate of hydroxyethyl ethylenediaminetriacetic acid [5] [Sn_2HEDTA]; monostannous chelate of nitrilotriacetic acid [6] [SnNTA]; monostannous chelate of iminodiacetic acid [7] [SnIDA]; and of N-substituted iminodiacetic acids such as monostannous chelate of N-methyl-, N-ethyl-, N-propyliminodiacetic acid, etc.; distannous chelate of propylenediaminetetraacetic acid [8]; distannous chelate of trimethylenediaminetetraacetic acid [9]; distannous chelate of tetramethylenediaminetetraacetic acid [10]; and generally the stannous chelates described in U. S. Patent 3,152,155. [Bracketed insertions ours.]

Appellant's specification also gives the following proposed theoretical explanation of how the invention operates:

> Unlike the stannous salts of the prior art, e.g., stannous fluoride and chloride, which are water soluble and unstable in aqueous media, or other chelates which are water soluble, unstable and too tightly chelated to be effective, the stannous chelates used in the dentifrices of this invention are substantially insoluble in water and stable in aqueous media and provide an effective source of stannous tin. The distannous chelate of ethylenediaminetetraacetic acid, for example, has a water solubility of less than 0.05 weight percent at room temperature and is stable in aqueous formulations. The low solubilfty in water contributes to the oxidation resistance of such chelates. In solution in saliva, the minor to trace amount of dissolved stannous chelate gives an acid reaction which, in the presence of naturally occurring chelating agents normally present in the mouth, such as sugars, proteins, amino acids and lactic acid, is believed to promote a reaction according to the following simplified equations:
>
> $SnR + R'H_2 \rightarrow SnR' + RH_2$
>
> $SnR' + H_2O \rightarrow SnOH^+ + HR'^-$
>
> In the equations, SnR represents a water-insoluble chelate as utilized in the dentifrices herein, $R'H_2$ represents a naturally occurring chelating agent normally present in the mouth, which compound has reactive hydrogen groups and the $SnOH^+$ cation represents a species which has been demonstrated polarographically to form by hydrolysis of tin(II) salts and complexes in aqueous solution; Acta Chemica Scandinavica, *12* (1958), 198-223. The $SnOH^+$ cation can react with the calcium hydroxyapatite of the enamel to form the insoluble basic stannous phosphate, in the same manner as stannous fluoride is believed now ultimately to react to form the same basic stannous phosphate. *Because of the complexities of the above reactions involving minute quantities of reactants, it has not yet been possible conclusively to demonstrate by present analytical techniques that such reactions do, in fact, take place.* Consequently, it is not desired to be bound by this theory, even though (1) the theory is consistent with all experimentally determined results, i.e., the formation with enamel of the basic stannous phosphate when a dentifrice containing one of the claimed stannous chelates is used and (2) such experimentally determined results are entirely consistent with said theory. *In any event, there is an exchange of the calcium of the enamel for stannous tin provided by the chelate.* As this exchange proceeds, a further minor to trace amount of stannous chelate dissolves and the exchange of stannous tin for calcium continues at the exposed surface of the tooth enamel while the dentifrice is in the mouth. Since the exposed tooth enamel surface in the mammalian mouth is relatively small, and the dentifrices are used on a continuing basis several times a day, an amount of stannous chelate as low as 0.00001 weight percent is effective in reducing enamel solubility. The exposure of enamel surfaces to the stannous chelates of the dentifrices herein described thus provides the tooth enamel with a surface of an insoluble basic stannous phosphate; J. of Dent. Res., *39*, 740, July-August 1960; [Myers,] J. Am. Dent. Assn., *77*, 1308, Dec. 1968. The compositions and methods disclosed are useful inter alia in the reduction of enamel solubility of valuable domesticated animals, such as, for example, dogs. [Emphasis and bracketed insertion ours.]

The specification contains sixteen "examples" of various types. Example 1 in the specification describes the results of a test where Sn_2EDTA (see note 4, supra) was added to the diet of separate groups of rats at levels of 200 parts per million (p.p.m.) for Group A, 300 p.p.m. for Group B, and none for Group C (control). At examination following sacrifice,

[4] Formula IVA, supra, when n is 2, represents this chelate.

[5] Formula IVB, supra, when n is 2, represents this chelate.

[6] Nitrilotriacetic acid is $N(CH_2COOH)_3$. The Condensed Chemical Dictionary, 619 (8th ed. 1971).

[7] Formula III, supra, represents this chelate.

[8] Formula IVA, supra, when $-(CH_2)n-$ is replaced by $-CH(CH_3)CH_2-$, represents this chelate.

[9] Formula IVA, supra, when n is 3, represents this chelate.

[10] Formula IVA, supra, when n is 4, represents this chelate.

Group A had 9.1 caries lesions (average) per animal and a tin level of 160 p.p.m. (average) in their tooth enamel, Group B had 7.5 caries lesions (average) per animal and a tin level of 225 p.p.m. (average) in their tooth enamel, and Group C (control) had 12.2 caries lesions (average) per animal and a tin level of 4 p.p.m. in their tooth enamel.

Example 2 describes a tooth paste formulation where "preferably 3% [by weight] of tin chelate, e.g., distannous ethylenediaminetetraacetic [Sn_2EDTA], is incorporated in this paste, but it can be varied from about 1% to about 15%." Example 3 describes another tooth paste formulation where "[t]o the paste is preferably added about 4% [by weight] of the tin chelate, distannous ethylenediaminetetraacetic [Sn_2EDTA]." Example 4 describes a tooth powder formulation containing 7.5 parts of Sn_2EDTA. Example 5 describes a mouth wash formulation containing Sn_2EDTA "to [the] limit of solubility." Example 6 describes an astringent mouth wash formulation containing Sn_2EDTA again "to [the] limit of solubility." Examples 7 and 8 describe chewing gum formulations containing Sn_2EDTA where the amount of the chelate "can be varied from about 0.00001% to about 15% by weight."

Example 9 describes a chewing gum formulation to which "five parts of stannous chelate of iminodiacetic acid [SnIDA, see note 7, supra] is added."

Example 10 describes a chewing gum formulation containing "twelve parts distannous chelate of propylene diaminetetraacetate [see note 8, supra]."

Example 11 describes a chewing gum in which the stannous chelates incorporated in the gum mix can be "distannous chelate of ethylenediaminetetraacetic acid [Sn_2EDTA]; distannous chelate of hydroxyethylethylenediaminetriacetic acid [Sn_2HEDTA, see note 5, supra]; monostannous chelate of nitrilotriacetic acid [SnNTA, see note 6, supra]; distannous chelate of propylenediaminetetraacetic acid [see note 8, supra]; distannous chelate of trimethylenediaminetetraacetic acid [see note 9, supra]; and distannous chelate of tetramethylenediaminetetraacetic acid [see note 10, supra]."

Examples 12 and 13 are both entitled "Artificial Mouth Test: Enamel Solubility Reduction." They are preceded by the following explanatory paragraph.

> To measure the effect on tooth enamel of enamel solubility reducing agents in dentifrices, dental researchers frequently use as an indicator the reduction in the amount of enamel dissolved or ESR test, as disclosed in Holliday et al. [Holliday], U. S. Patent 3,105,798, issued Oct. 1, 1963. Holliday et al. determined ESR following treatment of teeth with a dentifrice by measuring the decrease in amount of Ca^{45} and P^{32} dissolved from irradiated teeth by a measured volume of 0.1 N lactic acid-sodium lactate adjusted to a pH of 4.5. Another method for measuring ESR, the method used herein, is the lessened decrease in hardness of enamel, following exposure to one of the novel dentifrices herein described, when the enamel is dissolved in the artificial mouth with an acid pH buffered acetate solution or when it is dissolved in the artificial mouth by acid produced by an acid-producing streptococcus isolated from dental plaque; Pigman, W.: "In Vitro Production of Experimental Caries", J. Am. Dental Assn., *51* (1955), 685-696 (use of the artificial mouth in experimental caries research). Decrease in hardness of enamel due to solubilization or erosion of enamel was measured in following examples in Knoop units as determined with a Knoop diamond indenter using a Tukon hardness tester; W. T. Sweeney: "The Knoop Indentation Hardness Instrument as a Tool in Dental Research", J. Dent. Res. *21* (1942), 303; R. W. Phillips e.a., "Effect of Fluorides on Hardness of Tooth Enamel", J. Am. Dent. Assn. *37* (1948), 1; and T. Koulourides e.a., "Rehardening of Softened Enamel Surfaces of Human Teeth by Solutions of Calcium Phosphates", Nature, *189* (1961), 226-227. [Bracketed insertion ours.]

The test results stated in Examples 12 and 13 show that when human tooth enamel is exposed to solutions containing 1% by weight Sn_2EDTA the enamel softened and eroded less than the control samples.

Examples 14 and 15 describe tests where human subjects were fitted with bridge-like dental appliances holding small slabs of human teeth. The subjects then chewed sticks of chewing gum containing 1% and 0.01% by weight Sn_2EDTA for fifteen minutes three times each day for one week. Analysis of the slabs for tin uptake showed that they contained higher concentrations of stannous tin than the control slabs.

Finally, Example 16 describes a test using three groups "each of forty rats of mixed sex Osborne-Mendel caries-susceptible strain * * * maintained on a cariogenic diet * * *." Group (A) had applied to their teeth, twice each day for 115 days, a mixture of 3.5% by weight Sn_2EDTA in ORABASE emollient dental paste. Control group (B) had ORABASE emollient dental paste (without Sn_2EDTA) applied to their teeth, and control group (C) had nothing applied to their teeth. After sacrifice, examination of the rats' teeth showed that group (A), which had the Sn_2EDTA applied to their teeth, had "a caries reduction of approximately 40% as compared with the controls."

The Claimed Subject Matter

Claims 1-5 are drawn to dentifrices. Independent claim 1 recites generically a dentifrice as follows:

> 1. A dentifrice containing from about 0.00001 to 15 percent by weight of said dentifrice of a substantially water-insoluble stannous chelate of a chelating agent corresponding to the formula $(HOOCCH_2)_2NR$ wherein R is selected from the group consisting of H and $[(CH_2)n\text{-}N\text{-}(CH_2COOH)]m\text{-}CH_2COOH$ in which n is an integer from 2 to 4 and m is an integer from 0 to 4, wherein one or two of the $-CH_2COOH$ groups may be replaced by a $-CH_2CH_2OH$ group and wherein the Sn:N ratio of said chelate moiety is 1:1.

Dependent claims 2-5 recite dentifrices containing specific chelates as follows: (Bracketed insertions ours.)

> 2. A dentifrice as claimed in Claim 1 wherein the chelate is the distannous chelate of ethylenediaminetetraacetic acid [Sn_2EDTA].
>
> 3. A dentifrice as claimed in Claim 1 wherein the chelate is the stannous chelate of nitrilotriacetic acid [SnNTA].
>
> 4. A dentifrice as claimed in Claim 1 wherein the chelate is the stannous chelate of iminodiacetic acid [SnIDA].
>
> 5. A dentifrice as claimed in Claim 1 wherein the chelate is the distannous chelate of hydroxyethyl ethylenediaminetriacetic acid [Sn_2HEDTA].

Claims 6-10 are drawn to chewing gums. Independent claim 6 recites generically "[a] chewing gum containing from about 0.00001 to 15 percent by weight of said chewing gum of * * * [a chelate defined generically as in claim 1, supra]." Claims 7-10 are dependent on claim 6, and they recite chewing gums containing the specific chelates recited in claims 2-5, supra, respectively. For example, claim 7 reads as follows: (Bracketed insertion ours.)

> 7. A chewing gum as claimed in Claim 6 wherein the chelate is the distannous chelate of ethylenediaminetetraacetic acid [Sn_2EDTA].

Claims 11-20 are drawn to methods (processes) "whereby the enamel solubility is reduced." Independent claim 11 generically recites a method as follows:

> 11. Method which comprises contacting the enamel of teeth on a continuing basis with a substantially water-insoluble stannous chelate of a chelating agent corresponding to the formula $(HOOCCH_2)_2NR$ wherein R is selected from the group consisting of H and $[(CH_2)n\text{-}N\text{-}(CH_2COOH)\text{-}]m\text{-}CH_2COOH$ in which n is an integer from 2 to 4 and m is an integer from 0 to 4, wherein one or two of the $-CH_2COOH$ groups may be replaced by a $-CH_2CH_2OH$ group and wherein the Sn:N ratio of said chelate moiety is 1:1, whereby the enamel solubility is reduced.

Claims 12-15 are dependent on claim 11, and they recite methods wherein the chelates employed are the specific chelates recited in claims 2-5, supra, respectively. For example, claim 12 reads as follows: (Bracketed insertion ours.)

> 12. Method as claimed in Claim 11 wherein the chelate is the distannous chelate of ethylenediaminetetraacetic a[cid] [Sn_2EDTA].

Claim 16 is also dependent on claim 11, and it adds the further limitation that the method "comprises chewing a chewing gum containing from about 0.00001 to 15 percent by weight of * * * [a chelate defined generically as in claim 11, supra]." Claims 17-20 are dependent on claim 16, and they recite methods wherein the chewing gum contains the specific chelates recited in claims 2-5, supra, respectively. For example, claim 17 reads as follows: (Bracketed insertion ours.)

> 17. Method as claimed in Claim 16 wherein the chelate is the distannous chelate of ethylenediaminetetraacetic acid [Sn_2EDTA].

The References And The Rejection

The references relied on by the examiner and the board are:

Holliday et al. (Holliday) 3,105,798 Oct. 1, 1963 (filed May 29, 1958)

Fiscella 3,282,792 Nov. 1, 1966 (filed Jan. 9, 1964)

Griebstein 3,544,678 Dec. 1, 1970 (filed May 2, 1966)

Great Britain 922,385 Mar. 27, 1963 (filed Jan. 3, 1961)

Drug and Cosmetic Industry, 67:833 (Dec. 1950)

Langer, Journal of Dental Research, 39:740 (July-Aug. 1960)

Dental Abstracts, 8:372 (June 1963)

The references cited by appellant are:

Myers, J. Am. Dent. Assn., 77:1308-14 (Dec. 1968)

Norris et al. (Norris) 2,946,725 July 26, 1960 (filed Mar. 25, 1957)

Gagolski et al. (Gagolski) 3,471,613 Oct. 7, 1969 (filed Mar. 22, 1966)

Muhler 3,546,335 Dec. 8, 1970 (filed July 16, 1969)

In the final Office Action, claims 1-20 were rejected for "lack of proof of utility under 35

U.S.C. 101." The examiner's position was that the compositions and methods are "alleged to be useful in reducing enamel solubility of teeth in the mouth," but that "those skilled in the art would not accept applicant's allegation as obviously valid and correct." According to the examiner, the Drug and Cosmetic Industry reference [11] teaches "that stannous ion, when not in association with fluoride ion, is not effective in reducing dental caries"; the Holliday reference [12] teaches "that complexes of stannous tin and the chelating agent, ethylene diaminetetraacetic acid, are not suitable to supply tin ions in dentifrices since the tin is held too tightly"; the Fiscella reference [13] teaches "that stannous chelates of ethylene diaminetetraacetic acid have been found to be ineffective in dentifrices"; and the Langer reference [14] "indicates that the stannous chelates of the present invention failed to demonstrate a statistically significant lowering of dental caries when fed to rats." The examiner then stated that "* * * in the absence of clear and convincing evidence commensurate in scope with the allegation and claims, which evidence establishes the validity of the allegation, no claim can be indicated as allowable."

Appellant responded by submitting an affidavit executed by Mr. O. Ray McIntire, Technical Director of Research, Consumer Products Department of The Dow Chemical Company. McIntire's affidavit is 44 pages in length and gives in detail the results of numerous animal toxicity studies done on Sn_2EDTA. In addition, the affidavit states in detail the same tests and results described in Examples 12, 13, 14, 15 and 16 of appellant's specification, supra.

In the examiner's answer, three new references were cited "to show the state of the art": Griebstein,[15] British Patent 922,385, and Dental Abstracts. The examiner cited Griebstein and the British patent for this paragraph in Griebstein (col. 2, lines 28-35):

> Stannous chelates of alkylene polyamine carboxylic acid chelating agents such as ethylenediaminetetraacetic acid are disclosed for use in oral preparations in British Pat. 92,385 [sic; should read 922,385], published Mar. 27, 1963. *Such chelates have been found* to substantially impair the reactivity of stannous tin with dental enamel and are therefore of limited value in fluoride-containing oral compositions for caries prophylaxis. [Emphasis and bracketed insertion ours.]

British Patent 922,385, issued to The Dow Chemical Company, claims priority based on two U. S. patent applications, Ser. Nos. 43 and 78 (both filed Jan. 4, 1960), the former being the great-great-grandparent of the present application, and there is no question that the claimed subject matter includes the chelates disclosed in the British patent. In light of this teaching, the examiner thought that one skilled in the art would view appellant's allegations with a "great deal of skepticism," and he again stated that the § 101 rejection was proper "in the absence of clear and convincing evidence commensurate in scope with the allegations and claims * * *", citing In re Citron, 51 CCPA 852, 325 F.2d 248, 139 USPQ 516 (1963), In re Harwood, 55 CCPA 922, 390 F.2d 985, 156 USPQ 673 (1968), and In re Buting, 57 CCPA 777, 418 F.2d 540, 163 USPQ 689 (1969).

Responding to the McIntire affidavit, the examiner stated that the "Artificial Mouth Tests" (same as Examples 12 and 13 in the specification) fail "to establish the clinical effectiveness of the tested compound at the level tested." Relying on the newly cited Dental Abstracts reference,[16] the examiner stated that for clinical effectiveness to be established, the chemical agent should be subjected to clinical trials for two years if the agent is expected to arrest the progress of caries and for a longer time if the agent's effect in preventing caries is to be assessed. With regard to the tests described in the affidavit where subjects chewed gum containing 1% and 0.01% by weight Sn_2EDTA and the tin uptake in the test slabs was measured (same as Examples 14 and 15 in the specification), the examiner stated that this test was of "doubtful significance as no utility has been shown to result from the uptake of tin by dental enamel in the absence of fluoride." The examiner also criticized the test on the ground that it could not demonstrate utility for concentrations below those tested or for complexes other than the one tested. With respect to the test in the affidavit where a mixture of 3.5% by weight of Sn_2EDTA in ORA-BASE emollient dental paste was applied to the teeth of rats (same as Example 16 in the specification), the examiner criticized the test on the ground that it pertained to only one of the many complexes coming within the scope of the claims and that it was directed to a concentration far above the lowest level claimed. The examiner concluded by stating that no "clinical evidence relating to the reduction of caries is on the record" and "that the evidence appearing in the McIntire affidavit cannot establish the validity of the allegations."

In response to the newly cited Griebstein reference in the examiner's answer, an affidavit executed by Langer (the inventor in the present application) was submitted. Langer's affidavit states that he presented a paper on the enamel solubility reducing properties of Sn_2EDTA at a meeting of the International Association for Dental Research in March 1960. The affidavit states that two "representatives" of a certain domestic corporation (we have omitted names) were present and expressed interest in Sn_2EDTA; that one of the representatives wrote to Langer in May 1960 (a copy of the letter is attached to the affidavit) requesting a sample of Sn_2EDTA but such sample was not sent; that at the March 1961 meeting of the same association a third representative of the aforementioned domestic corporation reported that Sn_2EDTA had been tested "for in vitro solubility, i.e., distannous EDTA had been slurried in water and the supernatant aqueous liquid had been tested for dental enamel solubility reduction; it was notorious that * * * [the domestic corporation] was then looking for a tin reservoir compound which would deliver stannous ions to dentifrice pastes * * *;" and that Langer pointed out to the third representative that because of the chelate's low solubility in water, the supernatant aqueous liquid would not be expected to perform well, and certainly would not deliver any stannous ions to the toothpaste.

Langer's affidavit then makes the following statement regarding the Griebstein patent

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[11] Drug and Cosmetic Industry states in relevant part (col. 3, lines 1-25):

> Of pertinent interest are the experimental studies made by J. C. Muhler and H. G. Day (J. Am. Dent. Assoc. 41:529, 1950) on the effects of stannous fluoride, stannous chloride and sodium fluoride on the incidence of dental lesions in *rats* fed a caries-producing diet. They found that stannous fluoride in the concentration of ten parts of fluorine per million *in the drinking water* was greatly superior to sodium fluoride or stannous chloride in any concentration used in this experiment for reducing the incidence and severity of carious lesions in both strains of *rats. Stannous chloride did not appear to decrease significantly the incidence of dental caries.* Sodium fluoride in the concentrations of 10 ppm of fluorine in the drinking water had some preventive effect on the incidence and severity of the carious lesions. Neither the stannous salts nor the sodium fluoride had any apparent toxic effects in the concentrations used. [Emphasis ours.]

[12] Holliday states in relevant part (col. 3, lines 41-54):

> Many other compounds which form *water-soluble complexes* with metallic ions are known, but the aldonates [a complex of an aldonic acid such as gluconic acid] appear to be unique for the purposes of this invention. The complexing agent may be postulated to react with stannous ions to bind them tightly enough that their rate of becoming non-available to dental enamel by hydrolysis, oxidation, and precipitation is greatly reduced but not so tightly that they become non-available to dental enamel.
>
> Examples of complexers which bind the stannous ions more tightly than aldonates, and *which do not serve to achieve the objects of this invention, are* pyrophosphate, triphosphate, *ethylenediaminetetraacetate*, and phytate. Examples of complexers which apparently do not bind the stannous ions tightly enough are lactate and salicylate. [Bracketed insertion and emphasis ours.]

[13] Fiscella states in relevant part (col. 2, lines 7-18):

> The effect of the hydroxyl substituted aliphatic di- and tri-carboxylic acids [of Fiscella's invention] and their *water-soluble* salts *in preventing the precipitation and oxidation of the stannous ion* was unexpected. Compounds having characteristics similar to these acids *have been found* to be *ineffective for such purposes.* For instance, chelating and complexing agents, such as *ethylene diamine tetra-acetic acid* (known as EDTA and Versene), *have been found* to be *ineffective.* Yet the acids of the invention and their *water-soluble* salts effectively chelate or form a complex with the stannous ion which releases *stannous ion* in effective form in the mouth of the user. [Bracketed insertion and emphasis ours.]

[14] The Langer reference, authored by appellant, states (p. 740, item 249):

> Previous reports on caries inhibition have shown the importance of the stannous metal ion in SnF_2 [stannous fluoride] as well as the fluoride ion and the effectiveness of some metal ion chelates, including Zn, Ni, and Mn versenate. A new chemical, the distannous chelate of EDTA, has been prepared, which combines the effect of stannous ions with the advantages of the chelate—low toxicity and rate of hydrolysis as compared with other tin (II) salts. The compound has a surprisingly low solubility in water; yet, upon heating an aqueous slurry of dental enamel and the chelate for Ca/Sn 1/1, quantitative formation of a basic stannous phosphate takes place, corresponding with stannous fluoride treatments. Rat feeding tests by L. C. Hendershot, R. Mansell, and J. Forsaith (Biochem. Res. Lab., Dow Chemical Company) show a definite dose-response relationship for different amounts of stannous EDTA added to the cariogenic diet and a significant caries inhibition in female rats, *starting with a level of 200 ppm Sn.* A highly significant reduction in enamel solubility was obtained through treatment with Sn(II)$_2$EDTA by R. S. Manly (Westwood Research Laboratory). [Bracketed insertion and emphasis ours.]

[15] Griebstein had not issued at the time of the final Office Action.

[16] The Dental Abstracts reference is entitled "Clinical testing of cariostatic agents" and it states in relevant part:

> Before any cariostatic agent is subjected to clinical trial, preliminary experimental work should have determined its potential usefulness and safety. This usually involves in vitro tests, in vivo tests in animals, and small-scale pilot studies in humans. These data can be used to estimate the magnitude and variability of the cariostatic effect to be expected and the number of subjects required in a full-scale controlled study.
>
> * * *
>
> Clinical trials should be conducted for a minimum of two years if the agent is expected to arrest the progress of caries, but for a longer time if the agent's effect in preventing caries is to be assessed. There should be at least one year between re-examinations.

(which is assigned to the aforementioned domestic corporation):

> Langer, in reading U. S. patent 3,544,678 issued to Dr. Griebstein of * * * [the aforementioned domestic corporation], noted that Griebstein, by his attorney, inserted the following paragraph at * * * [col.] 2, * * * [lines] 28-35 of the said patent:
>
> "Stannous chelates of alkylene polyamine carboxylic acid chelating agents such as ethylenediaminetetra-acetic acid are disclosed for use in oral preparations in British Pat. 92,385, (this should be 922,385), published March 27, 1963. Such chelates have been found to substantially impair the reactivity of stannous tin with dental enamel and are therefore of limited value in fluoride-containing oral compositions for caries prophylaxis."; parenthetic insert added.
>
> This paragraph from Griebstein's patent is clearly mistaken, fails to indicate under what conditions any such chelate was used, and reminded Langer of past conversations had with * * * researchers [of the aforementioned domestic corporation], in particular * * * [the third representative of the domestic corporation], wherein it was reported that * * * [the domestic corporation] was attempting to use as a source of stannous ionic tin the chelate distannous EDTA in the form of a supernatant liquid obtained by slurrying some distannous EDTA with water, certainly not a source of stannous tin of any magnitude since the compound is substantially water insoluble and not a source of stannous ions, since the compound does not form stannous ions in water.

In his supplemental examiner's answer, the examiner stated that Langer's affidavit "contains no new evidence which would tend to convince those skilled in the art that the allegations in the specification are valid."

In affirming, the board said "* * * we agree with the examiner's rejection of the appealed claims as based upon lack of proof of utility (operativeness) of the claimed subject matter for its intended purpose (35 U.S.C. 101)." The board stated that appellant had the burden of supplying "evidence as to clinical testing which would resolve the issues in a simple manner."

The board found that the examiner's references (Holliday, Fiscella and Griebstein) provided an adequate basis for "skepticism," citing In re Ferens, 57 CCPA 733, 417 F.2d 1072, 163 USPQ 609 (1969). Considering the Myers reference cited by appellant, the board commented "[w]e are puzzled by the fact that the examiner has not discussed this article * * *," then proceeded to find that "Myers, in page 1312, column 2, first paragraph [17], clearly points out with respect to deposition of a related metal, lead, that reduction of enamel solubility (the 'ESR' test relied upon in appellant's arguments) is not directly correlated in clinical studies to a reduction of caries."

Concerning the three patents (Norris, Gagolski and Muhler) cited by appellant, the board said:

> The issuance by the Patent Office of the stated patents cannot establish a standard for the art to accept in vitro tests as demonstrating proof of utility in the human mouth with respect to living teeth. Numerous factors become important under the latter conditions, including the usual bacteria and other microorganisms and the continuous production of various fluids as well as intermittent contact with liquid and solid foods and environmental gases. We thus cannot consider in vitro tests alone to evidence actual utility. Compare * * * Hoover et al. v. Eckerd's Cut Rate Medical Co., Inc., 53 F.2d 215, 11 USPQ 55 [D. Del. 1931], affirmed 63 F.2d 813, 16 USPQ 327 [3rd Cir. 1933].

After considering appellant's petition for reconsideration, the board refused to change its decision.

Opinion

The question is whether the claimed subject matter is "useful" as required by the statement of "inventions patentable" found in 35 U.S.C. 101.[18]

[1] Preliminarily, it should be pointed out that the references relied on by the examiner and the board are not cited as "prior art" references. Indeed, the effective date, for prior art purposes, of many of these references is subsequent to appellant's earliest filing date. Rather, these references are properly cited for the purpose of showing a fact under the principle of In re Wilson, 50 CCPA 773, 311 F.2d 266, 135 USPQ 442 (1962). See In re Marzocchi, 58 CCPA 1069, n. 4, 439 F.2d 220, 169 USPQ 367 (1971).

Turning to the merits, the board held, apparently, that the examiner's references establish such a strong prima facie case for lack of utility ("usefulness") in the entire claimed subject matter that the highest type of evidence (i.e.—clinical testing in humans) is required to rebut the prima facie case.

Do the examiner's references establish a prima facie case for lack of utility in the entire claimed subject matter?

The Prima Facie Case For Lack of Utility

[2] As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented *must* be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter *unless* there is reason for one skilled in the art to question the objective truth of the statement of utility or its scope. Assuming that sufficient reason to question the statement of utility and its scope does exist, a rejection for lack of utility under § 101 will be proper on that basis; such a rejection can be overcome by suitable proofs indicating that the statement of utility and its scope as found in the specification are true. Cf. In re Marzocchi, 58 CCPA 1069, 1073, 439 F.2d 220, 223, 169 USPQ 367, 369 (1971) (involving the enablement requirement of 35 U.S.C. 112, first paragraph).

In the instant case, the Griebstein reference provides sufficient reason for one skilled in the art to question the objective truth of the statement of utility made for the entire claimed subject matter. Therefore, the examiner has established a prima facie case for lack of utility in the entire claimed subject matter.

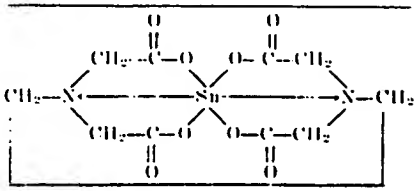
Appellant disputes the existence of a prima facie case. Citing the Langer publication (see note 14, supra), appellant argues that his preferred species, the distannous chelate of EDTA (Sn_2EDTA), is a novel chelate which was unknown at the time of Holliday's filing date, and that because it is insoluble in water (see also Langer's affidavit, supra), a person skilled in the art would know that Holliday and Fiscella are not referring to Sn_2EDTA, but rather they are referring to the chemically distinct *monostannous* chelate of EDTA [19] which is *soluble* in water. Although appellant's argument may be valid with respect to showing that Holliday and Fiscella do not establish a prima facie case for lack of utility for Sn_2EDTA, the argument fails with respect to Griebstein which specifically refers to the British patent (which discloses the *distannous* chelate of EDTA). Thus, insofar as Sn_2EDTA is concerned, Griebstein clearly provides sufficient reason to question appellant's statement of utility.

With regard to the remaining claimed species and the claimed genus (other than Sn_2EDTA), Griebstein also provides sufficient reason for one skilled in the art to question appellant's statement of utility. Griebstein refers to "[s]tannous chelates of alkylene polyamine carboxylic acid chelating agents," disclosed in British Pat. 922,385. This class of chelates disclosed in the British patent comprises a large portion of appellant's presently claimed genus. Griebstein then states that "*[s]uch chelates have been found* to substantially impair the reactivity of stannous tin with dental enamel and are therefore of limited value in fluoride-containing oral compositions for caries prophylaxis." (Emphasis ours.) Griebstein's pointed criticism of the class of chelates disclosed in the British patent is sufficient to establish a prima facie case for lack of utility in the remaining claimed species and in the claimed genus.

The Type of Evidence Needed to Rebut The Prima Facie Case

While we find that the Griebstein reference is sufficient to establish a prima facie case for lack of utility in the entire claimed subject matter, we do not agree with the board's view that clinical testing in humans is necessary here to rebut the prima facie case.

[3] It is not proper for the Patent Office to require clinical testing in humans to rebut a prima facie case for lack of utility when the pertinent references which establish the prima facie case show in vitro tests and when they do not show in vivo tests employing standard experimental animals.[20]



[17] The full paragraph reads as follows:

> Of the tin compounds that have been tried, only the stannous ion has been effective. The stannic ion has been proved to be inactive. Also related is the fact that the lead ion has been found to be extremely effective in reducing the solubility rate of apatite or dental enamel, although in three clinical studies it has been slightly active (30% reduction of caries) only once. From the clinical trials, whether precautions were taken to preserve the lead in the 2^+ state or whether its low solubility (0.06%) prevents concentrations high enough to be effective is not clear. In those studies in which the activity of lead has been assessed by the reduction of enamel solubility, it has generally been highly efficacious. [Footnote citations omitted].

[18] § 101. Inventions patentable

Whoever invents or discovers any new and *useful* process, machine, manufacture, or composition of matter, or any new and *useful* improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title. [Emphasis ours.]

[19] Appellant's brief gives the following chemical formula for the monostannous chelate of EDTA:

[20] We use the phrase "standard experimental animals" by way of analogy to In re Krimmel, 48 CCPA 1116, 1123, 292 F.2d 948, 953, 130 USPQ 215, 219 (1961), where it was defined as "whatever animal is usually used by those skilled in the art to establish the particular pharmaceutical application in question." See also In re Hartop, 50 CCPA 780, n. 14, 311 F.2d 249, 135 USPQ 419 (1962).

Although Holliday uses the phrase "do not serve" and Fiscella and Griebstein both use the phrase "have been found," these references do not indicate that their statements are supported by tests employing standard experimental animals, much less by clinical testing in humans.

Holliday does not disclose the basis for his statement regarding EDTA, but he discloses an in vitro enamel solubility reduction test to support the statement of utility for his claimed dentifrice invention.

Fiscella indicates that the experimental basis for his statement regarding EDTA is a simple in vitro test where an aqueous solution containing 0.50% by weight stannous fluoride and 2% by weight sodium salt of ethylenediaminetetraacetic acid is analyzed for stannous fluoride content after one week. (The ethylenediaminetetraacetic acid solution formed "a heavy precipitate" in one week and analysis showed that the amount of stannous fluoride in solution had dropped to nearly one half the original concentration in one week.)

Griebstein does not indicate the experimental basis for his statement regarding the "[s]tannous chelates of alkylene polyamine carboxylic acid chelating agents * * * disclosed * * * in British Pat. 92,385 [922,385] * * *." However, the disclosed experimental basis for the utility of Griebstein's invention is an in vitro tin uptake test employing tooth chips which are immersed in a slurry containing the dentifrice to be tested and then analyzed for tin.

Thus, the three pertinent references cited by the examiner use in vitro tests to support their own statements of utility, and one (Fiscella) clearly indicates that his statement regarding EDTA is based on an in vitro test. In such circumstances, it is reasonable to conclude that in vitro tests were used as the basis for all the statements regarding EDTA. Therefore, it was improper for the examiner and the board to require clinical testing in humans when the pertinent references only show in vitro tests.

Full scale clinical trials in humans, such as described in the Dental Abstracts reference (see note 16, supra), may be necessary to establish "commercial usefulness" in this technology. However, development of a product to the extent that it is presently commercially salable in the market place is not required to establish "usefulness" within the meaning of § 101. In re Anthony, 56 CCPA 1443, 414 F.2d 1383, 162 USPQ 594 (1969).

Claims 2, 7, 12 and 17

These claims are dependent claims which specifically recite a "dentifrice" (claim 2), a "chewing gum" (claim 7), or a "method" (claims 12 and 17) wherein the chelate is appellant's preferred species, the distannous chelate of ethylenediaminetetraacetic acid (Sn_2EDTA). Since these are dependent claims, they "* * * shall be construed to include all the limitations of the claim incorporated by reference into the dependent claim." 35 U.S.C. 112, second paragraph. We hold that the in vivo dental paste experiment (employing standard experimental animals) described in McIntire's affidavit, which verifies Example 16 of appellant's specification, is sufficient to rebut the prima facie case and to prove utility to one skilled in the art for Sn_2EDTA when employed in the claimed "dentifrice," "chewing gum," and "method."

Gagolski uses a dental paste experiment employing rats to show "cariostatic effect", and Muhler expressly states that rats are "standard experimental animals for anticariogenic studies." Hence, rats appear to be a standard experimental animal in this technology.

McIntire's affidavit, in verifying Example 16 of appellant's specification, states that a caries reduction of approximately 40% was achieved by brushing the rats' teeth with ORABASE emollient dental paste containing 3.5% by weight Sn_2EDTA. Brushing teeth, as described in the foregoing dental paste experiment, appears to be functionally equivalent to using chewing gum, since in both situations Sn_2EDTA contacts the tooth enamel. Hence, we accept the dental paste experiment employing a standard experimental animal as sufficient proof of utility for the subject matter recited in claims 2, 7, 12 and 17.

Appellant's dental paste experiment employing a standard experimental animal is clearly distinguishable from the simple in vitro "weighing" tests and "staining" tests described in Hoover v. Eckerd's Cut Rate Medicine Co., Inc., 53 F.2d 215, 11 USPQ 55 (D. Del. 1931), aff'd 63 F.2d 813, 16 USPQ 327 (3rd Cir. 1933).

The solicitor attacks appellant's dental paste experiment on three additional grounds. First, that the ORABASE material is not an "emollient dental paste" but rather a "denture adhesive." Second, that the 3.5% by weight Sn_2EDTA used in the verified test is insufficient proof for the claimed range of 0.00001 to 15% by weight. Third, that the rats may have received fluoride in their drinking water.

The problem regarding the identity or function of the ORABASE material stems from the fact that at one point in McIntire's affidavit, the affiant refers to ORABASE as a "denture adhesive" whereas in all other occurrences in the affidavit and in the specification, it is described as an "emollient dental paste." The solicitor has not asked us to take judicial notice of any product specification for ORABASE, and therefore the weight of the evidence favors the view that ORABASE is an "emollient dental paste." Furthermore, it is hard to see how the rats' teeth could be "brushed" using a denture adhesive, so the solicitor's argument is unrealistic.

The solicitor's argument regarding the range of 0.00001 to 15% by weight Sn_2EDTA fails to recognize the basic fact proved by the verified dental paste experiment. The basic fact proved by the experiment is that Sn_2EDTA is an active component in a dentifrice and that by using Sn_2EDTA a significant reduction in caries is achieved. Granted that 0.00001% by weight seems to be a very low concentration, but the Sn_2EDTA which will be present at that low concentration will nevertheless function in the intended way. A concentration of 0.00001% by weight Sn_2EDTA may not be commercially acceptable, but commercial acceptability is not required. See In re Anthony, supra, and Land v. Regan, 52 CCPA 1048, 342 F.2d 92, 144 USPQ 661 (1965).

McIntire's affidavit is silent on the subject of fluoride control, but it is fair to assume that the three groups of rats used in the experiment verified by McIntire were receiving the same drinking water. The two control groups should nullify any effect of fluorinated water insofar as the validity of the overall test is concerned, so the solicitor's argument on this ground must fail.

Claims 1, 3-6, 8-11, 13-16 and 18-20

These claims recite either the defined genus or species other than Sn_2EDTA. We hold that appellant's evidence of record is insufficient to rebut the prima facie case for lack of utility in the subject matter (other than Sn_2EDTA) recited in these claims.

Appellant's specification, supra, states that all members of the defined genus are substantially water insoluble, that all have an Sn to N ratio of 1 to 1, and that "all provide a source of tin reactive with tooth enamel * * *." However, as discussed earlier, the pertinent references provide sufficient reason for one skilled in the art to question this broad statement of utility.

To prove utility, appellant submitted McIntire's affidavit. But McIntire's affidavit describes experiments where the only chelate tested is Sn_2EDTA; thus, appellant has submitted no direct evidence proving utility for the other members of the defined genus.

In response to questions from the bench at oral hearing, appellant's counsel argued that the affidavit evidence for Sn_2EDTA was sufficient to prove indirectly the utility of the other claimed species and, therefore, the claimed genus. Counsel's basis for this argument was "the chemical structure of the compounds involved."

The issue is whether, in view of the prima facie case, one skilled in the art would accept the affidavit evidence for Sn_2EDTA as sufficient to prove indirectly the utility of the remaining members of the claimed genus (including the other claimed species).

[4] Appellant's argument seems to be that one skilled in this art would view similarity in structure as a reliable guide to functional equivalency for stannous chelates in dentifrices. Despite the fact that appellant had the burden of rebutting the prima facie case, appellant submitted no evidence to support the foregoing argument, and counsel's argument cannot take the place of evidence. See In re Schulze, 52 CCPA 1422, 346 F.2d 600, 145 USPQ 716 (1965), and In re Cole, 51 CCPA 919, 326 F.2d 769, 140 USPQ 230 (1964).

Moreover, Myers, cited by appellant, states that even the use of stannous fluoride in caries prevention rests on a "semi-empirical basis." This is some evidence that appellant is in a technology largely based on empirical results—not on predictable factors. See In re Cook, 58 CCPA 1049, 439 F.2d 730, 169 USPQ 298 (1971).

Therefore, since there is no evidence of record to support appellant's argument, we cannot say that one skilled in the art would accept the affidavit evidence for Sn_2EDTA as sufficient to prove indirectly the utility of the remaining members of the claimed genus. The prima facie case for lack of utility in the claimed subject matter (other than Sn_2EDTA) stands unrebutted.

In summary, we hold that appellant has submitted sufficient evidence to prove that claims 2, 7, 12 and 17 recite subject matter which is "useful" within the meaning of § 101, and therefore we reverse the board's decision on these claims. We further hold that appellant has not submitted sufficient evidence to prove that claims 1, 3-6, 8-11, 13-16 and 18-20 recite subject matter which is "useful," and therefore we affirm the board's decision on these latter claims.